Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A method of evaluating a compound, the method comprising

contacting a Silent Information Regulator (SIR) polypeptide having deacetylase activity with a compound in vitro, in the presence of a cytochrome c polypeptide substrate, wherein the amino acid sequence of the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:1 ~~an amino acid sequence of a SIR protein selected from the group consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7)~~, and

evaluating if the compound modulates interaction between the SIR polypeptide and the cytochrome c polypeptide substrate.

2. (Original) The method of claim 1, wherein the cytochrome c polypeptide is acetylated at at least one lysine.

3. (Currently Amended) The method of claim 1, wherein the cytochrome c polypeptide is a full length cytochrome c polypeptide.

4. (Previously Presented) The method of claim 1, wherein the cytochrome c polypeptide is human cytochrome c polypeptide.

5. – 7. (Canceled)

8. (Currently Amended) The method of claim 1, wherein the SIR polypeptide comprises the amino acid sequence of SEQ ID NO:1 ~~is SIRT1 (SEQ ID NO:1), SIRT2 (SEQ ID NO:2), or SIRT3 (SEQ ID NO:3)~~.

9. (Currently Amended) A method comprising:

contacting a cultured cell which expresses a SIR polypeptide having deacetylase activity and a cytochrome c polypeptide substrate with a test compound, wherein the amino acid sequence of the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:1 ~~an amino acid sequence of a SIR protein selected from the group consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7)~~, and

determining if the test compound modulates acetylation of the cytochrome c polypeptide substrate.

10. (Original) The method of claim 9 further comprising evaluating apoptosis or an indication of apoptosis in the cell.

11. (Currently Amended) A method of evaluating a test compound, the method comprising:

contacting a SIR polypeptide having deacetylase activity with a test compound, in the presence of a cytochrome c polypeptide substrate, in vitro, wherein the amino acid sequence of the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:1, ~~an amino acid sequence of a SIR protein selected from the group consisting of: SIRT1 (SEQ ID NO:1); SIRT2 (SEQ ID NO:2); SIRT3 (SEQ ID NO:3); SIRT4 (SEQ ID NO:4); SIRT5 (SEQ ID NO:5); SIRT6 (SEQ ID NO:6); and SIRT7 (SEQ ID NO:7), and~~

evaluating if the test compound modulates interaction between the SIR polypeptide and the cytochrome c polypeptide substrate;

contacting a cultured cell which expresses the SIR polypeptide and a cytochrome c polypeptide substrate with the test compound, and

determining if the test compound modulates acetylation of the cytochrome c polypeptide substrate in the cell.

12. – 22. (Canceled)

23. (Currently Amended) The method of claim 11 ~~claim 22~~, wherein the SIR polypeptide comprises the amino acid sequence of SEQ ID NO:1 ~~SIRT1 (SEQ ID NO:1)~~.

24. – 26. (Canceled)

27. (Previously Presented) The method of claim 1, wherein NAD or an NAD analog is present during the contacting step.

28. (Previously Presented) The method of claim 9, wherein NAD or an NAD analog is present during the contacting step.

29. – 30. (Canceled)

31. (Previously Presented) The method of claim 11, wherein NAD or an NAD analog is present during the contacting step.

32. – 33. (Canceled)

34. (New) The method of claim 9, wherein the SIR polypeptide comprises the amino acid sequence of SEQ ID NO:1.

35. (New) The method of claim 9, wherein the cytochrome c polypeptide is acetylated at at least one lysine.

36. (New) The method of claim 9, wherein the cytochrome c polypeptide is a full length cytochrome c polypeptide.

37. (New) The method of claim 9, wherein the cytochrome c polypeptide is human cytochrome c polypeptide.

38. (New) The method of claim 11, wherein the cytochrome c polypeptide is acetylated at at least one lysine.

39. (New) The method of claim 11, wherein the cytochrome c polypeptide is a full length cytochrome c polypeptide.

40. (New) The method of claim 11, wherein the cytochrome c polypeptide is human cytochrome c polypeptide.

41. (New) The method of claim 1, wherein the cytochrome c polypeptide is acetylated.

42. (New) The method of claim 9, wherein the cytochrome c polypeptide is acetylated.

43. (New) The method of claim 11, wherein the cytochrome c polypeptide is acetylated.

44. (New) A method of evaluating a compound, the method comprising

contacting a cultured cell which expresses a SIR polypeptide having deacetylase activity with a compound, in the presence of a cytochrome c polypeptide substrate, wherein the amino acid sequence of the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:1, and

evaluating if the compound modulates interaction between the SIR polypeptide and the cytochrome c polypeptide substrate.

45. (New) The method of claim 44, wherein the cytochrome c polypeptide is acetylated at at least one lysine.

46. (New) The method of claim 44, wherein the cytochrome c polypeptide is a full length cytochrome c polypeptide.

47. (New) The method of claim 44, wherein the cytochrome c polypeptide is human cytochrome c polypeptide.

48. (New) The method of claim 44, wherein the SIR polypeptide comprises the amino acid sequence of SEQ ID NO:1.

49. (New) The method of claim 44, wherein NAD or an NAD analog is present during the contacting step.

50. (New) The method of claim 44, wherein the cytochrome c polypeptide is acetylated.

51. (New) A method comprising:

contacting a SIR polypeptide having deacetylase activity and a cytochrome c polypeptide substrate with a test compound in vitro, wherein the amino acid sequence of the SIR polypeptide comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:1, and

determining if the test compound modulates acetylation of the cytochrome c polypeptide substrate.

52. (New) The method of claim 51, wherein NAD or an NAD analog is present during the contacting step.

53. (New) The method of claim 51, wherein the SIR polypeptide comprises the amino acid sequence SEQ ID NO:1.

54. (New) The method of claim 51, wherein the cytochrome c polypeptide is acetylated at at least one lysine.

55. (New) The method of claim 51, wherein the cytochrome c polypeptide is a full length cytochrome c polypeptide.

56. (New) The method of claim 51, wherein the cytochrome c polypeptide is human cytochrome c polypeptide.

57. (New) The method of claim 51, wherein the cytochrome c polypeptide is acetylated.